Zombie deer and the species barrier. Should humans worry about it?
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Abstract
This commentary reports of a deer chronic disease (chronic wasting disease - CWD), which might be transmitted to humans. It is due to a prion infection, similar to the bovine spongiform encephalopathy (BSE). At the moment, it is not known if the disease may be transmitted to humans. That is why all of us should be aware of the disease, and more careful while consuming deer meat.

Keywords
Chronic wasting disease (CWD); transmissible diseases; prions; spongiform encephalopathy

Chronic wasting disease (CWD) is a novel prion disease that in some parts of the United States affects up to 50% of free-ranging cervids and over 90% of certain captive herds [1]. It was first observed in 1967 but only recently has spread over broader areas and to larger populations. The search for Deer 0 has been fruitless, and it can only be speculated that CWD spontaneously occurred in a novel cervid prion or that it was in some way derived from scrapie that jumped the species barrier from ovine to cervid.

Animals with CWD hypersalivate and may exhibit ataxia, esophageal dilatation, regurgitation, and polyuria. CWD may have long incubation times, and the time from onset of symptoms to death may take months. Diseased animals have been observed to survive as long as a year [2].

Prions are misfolded proteins that can transmit their morphological abnormality to other proteins, which then aggregate into amyloids, accumulate in the neurological system, and lead to fatal outcomes without provoking an inflammatory response [3]. The misfolding results in massive structural damage to the prion and more visible conformational changes. Several prion diseases are known: Creutzfeld-Jacob disease, scrapie, and bovine spongiform encephalopathy (BSE or “mad cow disease”), all of which are transmissible spongiform encephalopathies, characterized by a long incubation period, progressive neuronal loss, and lethal outcome [2]. It is not known why prion diseases fail to provoke an immune response in the host. Unlike viruses or bacteria, prions cannot be inactivated, making them an indestructible and deadly pathogen that poses a potential public health risk. So far, CWD has remained confined to the animal kingdom.

CWD prions are shed in the urine and feces of infected animals, including animals that have no signs of the disease. These prions are remarkably persistent in the soil; reservoirs of infected prions exist in the wild and resist conventional disinfectants and other treatments [1]. It has been speculated that infected prions in the soil may be ingested by deer or be captured in dust particles that the animals inhale.

Among cervids, there is no species barrier to CWD infection but transmission to other animals appears limited [1]. Domestic and nondomestic felines, squirrel monkeys, and cynomolgus macaques have been experimentally infected with CWD by inoculation [4]. Under natural circumstances, CWD transmission has occurred in opossums, [5] while raccoons appear to have a natural resistance [3]. Since BSE is a prion disease that was effectively transmitted to humans who handled or ate meat infected beef, the question arises as to whether or not CWD could affect humans.

Cross-species transmissions require certain cellular similarities [6]. An invading prion conformer may carry disease if it has certain structural features, the most important of which are the loop region between the β-sheet 2 and α-helix 2 [7]. Humans have prion proteins with an unstructured N-terminus and a globular C-terminus; the protein segment involving the β-2 loops and the α-2 helices differ among species and are thought to play a role in disease transmission. Thus, current thinking is that the risk of CWD infecting humans is low, but cannot be ruled out [8].

Prion replication in the absence of DNA and RNA remains to be elucidated, but greater insights into this could lead to better understanding of other neurological conditions, such as Alzheimer disease, Parkinson disease, and amyotrophic lateral sclerosis. BSE etiology appears to be based - at least in part - on conformational alterations of the prion, which suggests that the host may play a role in how prion disease develops by way of biochemical interactions between pathogenic prions and healthy proteins. Prions are not homogenous and “prion strain phenomenon” suggests that certain infective prions may propagate as structurally unique strains with their own specific biological and biochemical characteristics. In other words, the primary prion sequencing of both donor and recipient may
affect prion misfolding. If this is true, it implies the infective prion is both versatile and adaptable, which may facilitate its transmission to some species but not others. This speculated adaptability raises concern about the zoonotic potential of CWD. Up to now, CWD in its current form has been thwarted by the species barrier from reaching humans, but round-about variations (from deer to intermediate animal to human) could circumvent this barrier and lead to a deadly prion disorder with the potential to affect humans. Moreover, the potential human infection eating deer meat cannot be excluded.

The animals with advanced CWD are sometimes called “zombie deer,” because they become disoriented, lose coordination, drool copiously, and grow emaciated. It is not known if or how CWD can be stopped in the free-ranging deer populations of North America, nor it is known if this disease will spread among all deer, whether it may infect other animals, and if it might one day, like BSE, be able to infect humans. For these reasons, it seems imperative to better understand CWD and to elevate awareness about it. For example, it is important that hunters not eat venison or meat from certain areas where CWD deer roam, even if the animal processed showed no symptoms. While CWD tests for venison are available, they are not advanced enough to be considered reliable food safety tests.

A lack of a reliable CWD test for a living animal, free-ranging herds, and a long incubation period make it difficult to identify infected animals and their herds. Clearly infected animals can be destroyed, but it may not be possible to stop CWD in the wild. This represents a zoological and ecological tragedy that may eventually have serious consequences if CWD is able to expand its territory, not just among wild animals but also to humans. As physicians and scientists, we must be mindful of this disease now, in its current form, and be prepared in case it may morph into a disease with the potential to infect humans. This should not become a new potentiality for epidemics, and increased necessities of health care support, eventually in the intensive care settings.